

Please amend the application as follows:

In the Claims

Please cancel non-elected Claims 1-9, 23, 33-39 and 47-62 without prejudice to their prosecution in any related or subsequently filed application by Applicants. Please amend Claims 16, 17, 19-22, 24, 30, 32, 40, 42, 45 and 46.

- B1/2*
16. (Amended) A method for regulating delivery of oxygen and NO⁻, in various redox forms,] in a mammal, comprising administering to the mammal an effective amount of a mixture of a low molecular weight thiol or nitrosothiol and hemoglobin or nitrosated hemoglobin[⁻, selected for the oxidation state of the heme iron and for the oxygenation state].
17. (Amended) A method for delivering NO in a mammal, comprising administering to the mammal an effective amount of a blood substitute comprising nitrosated hemoglobin.
- B2*
19. (Amended) A method for scavenging oxygen free radicals and NO⁻ in a mammal, comprising administering to the mammal an effective amount of a blood substitute comprising nitrosated hemoglobin.
20. (Amended) A method for reducing blood pressure in a mammal, comprising administering an effective amount of nitrosated hemoglobin to the mammal.
21. (Amended) A method for treating a disease in a mammal, comprising administering an effective amount of [a form of] nitrosated or nitrated hemoglobin to the mammal, wherein the disease is selected from the group consisting of heart disease, brain disease, vascular disease, atherosclerosis, lung disease and inflammation.
22. (Amended) A method for treating a medical condition in a mammal, comprising administering an effective amount of [a form of] nitrosated hemoglobin to the mammal, wherein the medical condition is selected from the group consisting of stroke, angina and acute respiratory distress.

- B3
24. (Amended) A method for treating a human with sickle cell anemia comprising administering to the human an effective amount of a preparation comprising -S-NO-Hb(FeII)O₂.
- B4
30. (Amended) A method for treating a disorder resulting from platelet activation or adherence in an animal or human, comprising administering an effective amount of a composition comprising nitrosated or nitrated hemoglobin in a therapeutically effective amount.
- B5
32. (Amended) A method for preventing thrombus formation in an animal or human, comprising administering an effective amount of a composition comprising nitrosated hemoglobin in a therapeutically effective amount.
- B6
40. (Amended) Method for [treating or preventing a disease or medical disorder which can be ameliorated by delivery of] delivering NO or its biological equivalent to tissues [affected by the disease or medical disorder,] in an animal or human, comprising administering to the animal or human an effective amount of one or more nitrosyl-heme-containing donors of NO.
- B7
42. (Amended) Method for making stable [nitrosyl-deoxyhemoglobin] nitrosylhemoglobin comprising adding NO to deoxyhemoglobin in an aqueous solution such that the ratio of NO:heme is less than about 1:100 [or greater than about 0.75].
- B8
45. (Amended) A composition comprising [nitrosyl-deoxyhemoglobin] nitrosylhemoglobin in a physiologically compatible buffer, wherein the ratio of NO:heme is less than about 1:100 [or greater than about 0.75].
- 5MB
46. (Amended) Method for making [nitrosyl-oxyhemoglobin] S-nitrosohemoglobin comprising adding NO to oxyhemoglobin in an aqueous solution such that the ratio of NO:hemoglobin is less than about 1:30.

Please add Claims 63-68.

- (d)* 63. A method for producing SNO-hemoglobin, said method comprising mixing nitric oxide and deoxyhemoglobin at pH 7.4 and exposing the resulting solution to air.
- (d)* 64. A method for producing nitrosylhemoglobin, said method comprising mixing nitric oxide with deoxyhemoglobin at pH 7.4 under anaerobic conditions at a heme:NO ratio of greater than about 14.
- (d)* 65. A method for producing S-nitrosohemoglobin, said method comprising mixing nitric oxide and oxyhemoglobin in aqueous buffer at pH 7.4.
- (d)* 66. The method of Claim 65 wherein the oxyhemoglobin is greater than about 18 μM .
- (d)* 67. A method for making stable nitrosylhemoglobin comprising adding NO to deoxyhemoglobin in an aqueous solution such that the heme:NO ratio is at least about 70:1.
- (d)* 68. A composition comprising nitrosylhemoglobin in a physiologically compatible buffer, wherein the heme:NO ratio is at least about 70:1.

REMARKS

Claims 1-9, 23, 33-39 and 47-62 have been canceled. Claims 16,17, 19-22, 24, 30, 32, 40, 42, 45 and 46 have been amended. Claims 63-68 have been added.

Support for addition of the phrase "an effective amount of" in the claims can be found at page 40, lines 22-26 and on page 40, line 34 to page 41, line 22. Support for the amendment of Claim 46 can be found in Example 21 at page 77, lines 20-24, for example.

Support for Claim 63 is found on page 72, lines 25-31, for example. Support for Claim 64 can be found at page 73, lines 14 to page 74, line 9 and in Figures 14A and 14B. Support for Claim 65 can be found in Example 19, page 75, line 29, to page 76, line 6, and in Figure 17. For